

What is claimed is:

1. A composition comprising a stabilized Exendin-4 (1-39) comprising:
 - a) a deletion of 0 to 5 amino acids at positions corresponding to positions 34-38 of Exendin-4,
 - 5 b) optionally, at least one peptide sequence Z comprising 4-20 amino acid units covalently bound to said compound; and at least one of the following:
 - i) an Asn residue having a deaminated side chain, an Asn residue having hydrolyzed side chain or a structural isomer of an Asp residue, wherein the Asn or Asp residue corresponds to position 28 of Exendin-4,
 - 10 ii) an oxidized methionine residue corresponding to position 14 of Exendin-4,
 - iii) an oxidized tryptophan residue corresponding to position 25 of Exendin-4; and
 - iv) a deaminated or hydrolyzed Gln corresponding to position 13 of Exendin-4 and a pharmaceutically acceptable salt or solvate thereof.
- 15 2. The composition of claim 1, wherein the Asn residue is an α -aspartate (Asp) or β -aspartate (isoaspartyl) residue.
3. The composition of claim 1, wherein the Asn residue is an Cyclic imide such as an aspartimide or glutimide.
- 20 4. The composition of claim 1, wherein the oxidized methionine residue is a methioninyl sulfoxide or a methioninyl sulfone.
5. The composition of claim 1, wherein the oxidized tryptophan residue comprises an oxidized 3H-indol-3-yl group.
- 25 6. The composition of claim 1, wherein the oxidized tryptophan residue is N-formylkynurenine (NFK), 3-hydroxykynurenine (3-OH-KYN), hydroxytryptophan (HTRP), or kynurenine (KYN).
- 30 7. The composition of claim 1, wherein Z comprises at least one Lys amino acid unit.
8. The composition of claim 7, wherein Z comprises between about 4 to about 20 Lys amino acid units.

9. The composition of claim 8, wherein Z comprises about 6 Lys amino acid units.
10. The composition of claim 1, wherein the stabilized Exendin-4 (1-39) compound and Z are covalently bound by a peptide bond.
- 5 11. The composition of claim 1, wherein Z is covalently bound to the stabilized Exendin-4 (1-39) compound at the C-terminal carbonyl function.
12. The composition of claim 1, wherein the stabilized Exendin-4 (1-39) compound
10 comprises any one of the following sequences:
des Pro³⁶[Asp²⁸]Exendin-4 (1-39),
des Pro³⁶[IsoAsp²⁸]Exendin-4 (1-39),
des Pro³⁶[Cyclic imide²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴]Exendin-4 (1-39), or
15 des Pro³⁶[Trp(O₂)²⁵]Exendin-4 (1-39).
13. The composition of claim 12 further comprising the following group linked to the C-terminus of the compound: -Lys₆-NH₂.
- 20 14. The composition of claim 1, wherein the stabilized Exendin-4 (1-39) compound comprises any one of the following sequences:
des Pro³⁶[Met(O)¹⁴, Asp²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, IsoAsp²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, Cyclic imide²⁸]Exendin-4 (1-39), or
25 des Pro³⁶[Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4 (1-39).
15. The composition of claim 14 further comprising the following group linked to the C-terminus of the compound: -Lys₆-NH₂.
- 30 16. The composition of claim 1, wherein the stabilized Exendin-4 (1-39) compound comprises any one of the following sequences:
des Pro³⁶[Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
des Pro³⁶[Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39) or
des Pro³⁶[Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39).

17. The composition of claim 16 further comprising the following group linked to the C-terminus of the compound: -Lys₆-NH₂.
18. The composition of claim 1, wherein the stabilized Exendin-4 (1-39) compound
 5 comprises any one of the following sequences:
 des Pro³⁶[Met(O)¹⁴ Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
 des Pro³⁶[Met(O)¹⁴ Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39), or
 des Pro³⁶[Met(O)¹⁴ Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39).
19. The composition of claim 18 further comprising the following group linked to the C-terminus of the compound: -Lys₆-NH₂.
20. The composition of claim 1, wherein the stabilized Exendin-4 (1-39) compound
 15 comprises any one of the following sequences:
 H-(Lys)₆- des Pro³⁶[Asp²⁸]Exendin-4(1-39)-Lys₆-NH₂
 des Asp²⁸ Pro³⁶, Pro³⁷, Pro³⁸Exendin-4(1-39) -NH₂,
 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸[Asp²⁸]Exendin-4(1-39) -NH₂
 H-Asn-(Glu)₅ des Pro³⁶, Pro³⁷, Pro³⁸[Asp²⁸]Exendin-4(1-39) -NH₂,
 des Pro³⁶, Pro³⁷, Pro³⁸[Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 20 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸[Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸[Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,

 H-(Lys)₆- des Pro³⁶[Cyclic imide²⁸]Exendin-4(1-39)-Lys₆-NH₂,
 des Pro³⁶, Pro³⁷, Pro³⁸[Cyclic imide²⁸]Exendin-4(1-39)-NH₂,
 25 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸[Cyclic imide²⁸]Exendin-4(1-39) -NH₂
 H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸[Cyclic imide²⁸]Exendin-4(1-39)-NH₂,
 des Pro³⁶, Pro³⁷, Pro³⁸[Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 H-(Lys)₆ des Pro³⁶, Pro³⁷, Pro³⁸[Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸[Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 30
 H-(Lys)₆- des Pro³⁶[Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-Lys₆-NH₂,
 H- des Asp²⁸ Pro³⁶, Pro³⁷, Pro³⁸[Trp(O₂)²⁵]Exendin-4(1-39) -NH₂,
 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸[Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39) -NH₂,
 H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸[Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39) -NH₂,

- des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
- 5 H-(Lys)₆- des Pro³⁶ [Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-Lys₆-NH₂,
des Cyclic imide²⁸ Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵]Exendin-4(1-39)-NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39) -NH₂,
H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-NH₂,
des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
- 10 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
H-Asn-(Glu)₅-des Pro³⁶, Pro³⁷, Pro³⁸ [Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-
NH₂,
- H-(Lys)₆- des Pro³⁶ [Met(O)¹⁴, Asp²⁸]Exendin-4(1-39)-Lys₆-NH₂,
- 15 des Met(O)¹⁴Asp²⁸Pro³⁶, Pro³⁷, Pro³⁸ Exendin-4(1-39) -NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Asp²⁸]Exendin-4(1-39) -NH₂,
H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Asp²⁸] Exendin-4(1-39) -NH₂,
des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
- 20 H-Asn-(Glu)₅ des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
- H-Lys₆- des Pro³⁶ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39)-Lys₆-NH₂,
des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39)-NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39) -NH₂,
- 25 H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39)-NH₂,
des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-
NH₂,
- 30 H-Lys₆- des Pro³⁶ [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-Lys₆-NH₂,
H- des Asp²⁸Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4(1-39) -NH₂,
H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39) -NH₂,
H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39) -NH₂,

des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 H-Asn-(Glu)₅-des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4(1-39)-(Lys)₆-
 NH₂,

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H-Lys₆- des Pro³⁶ [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-Lys₆-NH₂,
 des Cyclic imide²⁸ Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵] Exendin-4(1-39)-NH₂,
 H-(Lys)₆- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39) -
 NH₂,

10 H-Asn-(Glu)₅- des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-
 39)-NH₂,

des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-(Lys)₆-NH₂,
 H-(Lys)₆-des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-
 (Lys)₆-NH₂,

15 H-Asn-(Glu)₅-des Pro³⁶, Pro³⁷, Pro³⁸ [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4(1-39)-
 (Lys)₆-NH₂,

or a pharmaceutically acceptable salt or solvate thereof.

21. A composition comprising a stabilized Exendin-4 (1-39) compound comprising at
 20 least one of:

- i) an Asn residue having a deaminated side chain, an Asn residue having hydrolyzed side chain or a structural isomer of an Asp residue, wherein the Asn or Asp residue corresponds to position 28 of Exendin-4,
- ii) an oxidized methionine residue corresponding to position 14 of Exendin-4,
- 25 iii) an oxidized tryptophan residue corresponding to position 25 of Exendin-4; and
- iv) a deaminated or hydrolyzed Gln corresponding to position 13 of Exendin-4 and a pharmaceutically acceptable salt or solvate thereof.

22. The composition of claim 21, wherein the stabilized Exendin-4 (1-39) compound
 30 comprises any one of the following sequences:

[Asp²⁸]Exendin-4 (1-39),
 [IsoAsp²⁸]Exendin-4 (1-39),
 [Cyclic imide²⁸]Exendin-4 (1-39),
 [Met(O)¹⁴]Exendin-4 (1-39), or

[Trp(O₂)²⁵]Exendin-4 (1-39).

23. The composition of claim 21, wherein the stabilized Exendin-4 (1-39) compound comprises any one of the following sequences:

- 5 [Met(O)¹⁴, Asp²⁸]Exendin-4 (1-39)
[Met(O)¹⁴, IsoAsp²⁸]Exendin-4 (1-39),
[Met(O)¹⁴, Cyclic imide²⁸]Exendin-4 (1-39), or
[Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4 (1-39).

10 24. The composition of claim 21, wherein the compound comprises any one of the following sequences:

- [Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
[Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39) or
[Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39).

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25. The composition of claim 21, wherein the compound comprises any one of the following sequences:

- [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39)
[Met(O)¹⁴, Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39), or
20 [Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39).

26. The composition of claim 1 or 21, wherein the amino acid residues have an L-configuration, a D-configuration, or the composition includes a mixture of L- and D-amino acid residues.

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27. A pharmaceutically acceptable composition comprising at least one of the stabilized Exendin-4 (1-39) compounds of claims 1 to 26.

28. The pharmaceutically acceptable composition of claim 27, wherein the composition
30 comprises a depot formulation, microspheres, liposomes or the composition includes a stabilized liquid formulation.

29. The pharmaceutically acceptable composition of claim 27, wherein the composition comprises at least one of the following compounds:

des Pro³⁶[Asp²⁸]Exendin-4 (1-39),
des Pro³⁶[IsoAsp²⁸]Exendin-4 (1-39),
des Pro³⁶[Cyclic imide²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴]Exendin-4 (1-39),
5 des Pro³⁶[Trp(O₂)²⁵]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, Asp²⁸]Exendin-4 (1-39)
des Pro³⁶[Met(O)¹⁴, IsoAsp²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, Cyclic imide²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4 (1-39),
10 des Pro³⁶[Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
des Pro³⁶[Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39),
des Pro³⁶[Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4 (1-39),
des Pro³⁶[Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
15 des Pro³⁶[Met(O)¹⁴, Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39), and
des Pro³⁶[Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39).

30. The pharmaceutically acceptable composition of claim 29 further comprising the following group linked to the C-terminus of the compound: -Lys₆-NH₂

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31. The pharmaceutically acceptable composition of claim 27, wherein the composition comprises at least one of the following compounds:

[Asp²⁸]Exendin-4 (1-39),
[IsoAsp²⁸]Exendin-4 (1-39),
25 [Cyclic imide²⁸]Exendin-4 (1-39),
[Met(O)¹⁴]Exendin-4 (1-39),
[Trp(O₂)²⁵]Exendin-4 (1-39),
[Met(O)¹⁴, Asp²⁸]Exendin-4 (1-39)
[Met(O)¹⁴, IsoAsp²⁸]Exendin-4 (1-39),
30 [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4 (1-39),
[Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4 (1-39)
[Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
[Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39),
[Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39),

Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
[Met(O)¹⁴, Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39); and
[Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39)

- 5 32. A pharmaceutically acceptable composition comprising Exendin-4 (1-39) or a variant, analogue or derivative thereof, the composition further comprising at least one of the following stabilized Exendin-4 compounds:

[Asp²⁸]Exendin-4 (1-39),
[IsoAsp²⁸]Exendin-4 (1-39),
10 [Cyclic imide²⁸]Exendin-4 (1-39),
[Met(O)¹⁴]Exendin-4 (1-39),
[Trp(O₂)²⁵]Exendin-4 (1-39),
[Met(O)¹⁴, Asp²⁸]Exendin-4 (1-39),
[Met(O)¹⁴, IsoAsp²⁸]Exendin-4 (1-39),
15 [Met(O)¹⁴, Cyclic imide²⁸]Exendin-4 (1-39),
[Met(O)¹⁴, Trp(O₂)²⁵]Exendin-4 (1-39)
[Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
[Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39),
[Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39),
20 [Met(O)¹⁴, Trp(O₂)²⁵, Asp²⁸]Exendin-4 (1-39),
[Met(O)¹⁴, Trp(O₂)²⁵, IsoAsp²⁸]Exendin-4 (1-39), and
[Met(O)¹⁴, Trp(O₂)²⁵, Cyclic imide²⁸]Exendin-4 (1-39).

- 25 33. The pharmaceutically acceptable composition of claim 32, wherein the weight ratio of the stabilized Exendin-4 (1-39) to the Exendin-4 (1-39) or the variant, analogue or derivative thereof is less than about 50% (w/w).

34. The pharmaceutically acceptable composition of claim 33, wherein the weight ratio of the stabilized Exendin-4 (1-39) to the Exendin-4 (1-39) or the variant, analogue or
30 derivative thereof is less than about 10% (w/w).

35. The pharmaceutically acceptable composition of claim 34, wherein the weight ratio of the stabilized Exendin-4 (1-39) to the Exendin-4 (1-39) or the variant, analogue or derivative thereof is less than about 1% (w/w).

36. A method of making the composition of claim 1 comprising at least one of the following steps:

a) obtaining Exendin-4 (1-39) or a variant, analogue, or derivative thereof; and

5 b) incubating the Exendin-4 (1-39) or the variant, analogue, or derivative thereof under conditions sufficient to introduce at least one of the following amino acids therein:

10 i) an Asn residue having a deaminated side chain, an Asn residue having hydrolyzed side chain or a structural isomer of an Asp residue, wherein the Asn or Asp residue corresponds to position 28 of Exendin-4,

ii) an oxidized methionine residue corresponding to position 14 of Exendin-4,

iii) an oxidized tryptophan residue corresponding to position 25 of Exendin-4; and

iv) a deaminated or hydrolyzed Gln corresponding to position 13 of Exendin-4.

15 37. The method of claim 36 further comprising the step of detecting presence or absence of at least one of amino acids (i)-(iv).

38. The method of claim 37, further comprising the step of identifying at least one of the amino acids (i)-(iv) in the composition.

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39. A method of making the composition of claim 27 comprising at least one of the following steps:

a) obtaining Exendin-4 (1-39) or a variant, analogue or derivative thereof,

25 b) contacting the Exendin-4 (1-39) or the variant, analogue or derivative with at least one pharmaceutically acceptable carrier or vehicle to produce a mixture; and

c) incubating the mixture under conditions sufficient to introduce at least one of the following amino acids therein:

30 i) an Asn residue having a deaminated side chain, an Asn residue having hydrolyzed side chain or a structural isomer of an Asp residue, wherein the Asn or Asp residue corresponds to position 28 of Exendin-4,

ii) an oxidized methionine residue corresponding to position 14 of Exendin-4,

iii) an oxidized tryptophan residue corresponding to position 25 of Exendin-4; and

iv) a deaminated or hydrolyzed Gln corresponding to position 13 of Exendin-4.

40. The method of claim 39 further comprising detecting presence or absence of at least one of the amino acid residues (i)-(iv).
41. The method of claim 40, further comprising the step of identifying at least one of the amino acids (i)-(iv) in the composition.
42. The method of claim 40, wherein the conditions include contact with at least one of water, heat, light, metal, metal ions, water vapor or oxygen.
43. The method of claim 42, wherein the conditions further include contact with about room temperature (25°C).
44. The method of claim 43, wherein the conditions further include contact with air.
45. A method of stabilizing Exendin-4 (1-39) or a variant, analogue or derivative thereof from degradation before, during or after intended use, said method comprising at least one of the following steps:
- a) obtaining Exendin-4 (1-39) or a variant, derivative or analogue thereof; and
 - b) incubating the Exendin-4 (1-39) or the variant, derivative or analogue under conditions sufficient to introduce at least one of the following amino acid residues therein:
 - i) an Asn residue having a deaminated side chain, an Asn residue having hydrolyzed side chain or a structural isomer of an Asn residue, wherein the Asn residue corresponds to position 28 of Exendin-4,
 - ii) an oxidized methionine residue corresponding to position 14 of Exendin-4,
 - iii) an oxidized tryptophan residue corresponding to position 25 of Exendin-4
 - iv) a deaminated or hydrolyzed Gln corresponding to position 13 of Exendin-4.
46. The method of claim 45, wherein the conditions include contact with at least one of water, heat, light, metal, metal ion, water vapor or oxygen.
47. The method of claim 46, wherein the conditions include contact with about room temperature (25°C).

48. The method of claim 46, wherein the conditions further include contact with air.

49. The method of claim 45, further comprising the step of detecting presence or absence of at least one of the amino acid residues (i)-(iv).

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50. The method of claim 49, further comprising the step of identifying at least one of the amino acids (i)-(iii) in the stabilized Exendin-4 (1-39) or variant, analogue or derivative thereof.

10 51. The method of claim 45, the method further comprising contacting the stabilized Exendin-4 (1-39) or variant, derivative or analogue thereof with at least one pharmaceutically acceptable carrier or vehicle.

15 52. A method for treating diabetes type 1 or type 2, insulin resistance syndrome, impaired glucose tolerance (IGT), obesity, eating disorders, hyperglycemia, metabolic disorders, and gastric disease, the method comprising administering a therapeutically effective amount of at least one of the compositions of claims 1 to 51.

20 53. A method for treating disease states associated with elevated blood glucose levels, said method comprising administering a therapeutically effective amount of at least one of the compositions of claims 1 to 51.

25 54. A method for regulation of blood glucose levels, the method comprising administering a therapeutically effective amount of at least one of at least one of the compositions of claims 1 to 51.

55. A method for regulation of gastric emptying, the method comprising administering a therapeutically effective amount of at least one of the compositions of claims 1 to 51.

30 56. A method of stimulating insulin release in a mammal comprising administering an effective Insulinotropic amount of at least one of the compositions of claims 1 to 51.

57. A method of lowering blood glucose level in a mammal comprising administering an amount of at least one of the compositions of claims 1 to 51 effective to lower blood glucose level in said mammal.
- 5 58. A method of lowering plasma lipid level in a mammal comprising administering an amount of at least one of the compositions of claims 1 to 51 effective to lower plasma lipid level in said mammal.
- 10 59. A method of reducing mortality and morbidity after myocardial infarction in a mammal comprising administering an amount of at least one of the compositions of claims 1 to 51 effective to reduce mortality and morbidity after myocardial infarction.
60. A method of stimulating insulin release in a mammal comprising administering an effective insulintropic amount of at least one of the compounds of claims 1 to 51.
- 15 61. A method of lowering blood glucose level in a mammal comprising administering an amount of at least one of the compounds of claims 1 to 51 effective to lower blood glucose level in said mammal.
- 20 62. A method of lowering plasma lipid level in a mammal comprising administering an amount of at least one of the compounds of claims 1 to 51 effective to lower plasma lipid level in said mammal.
63. The method of any one of claims 52-62, wherein the mammal is a human patient.
- 25 64. A method of making a stabilized Exendin (1-39) of the invention, the method comprising synthesizing the compound in an automated or semi-automated format.
65. The method of claim 64, wherein the synthesis involves the Merrifield technique.
- 30 66. A stabilized Exendin (1-39) made by the methods of claims 64-65.